

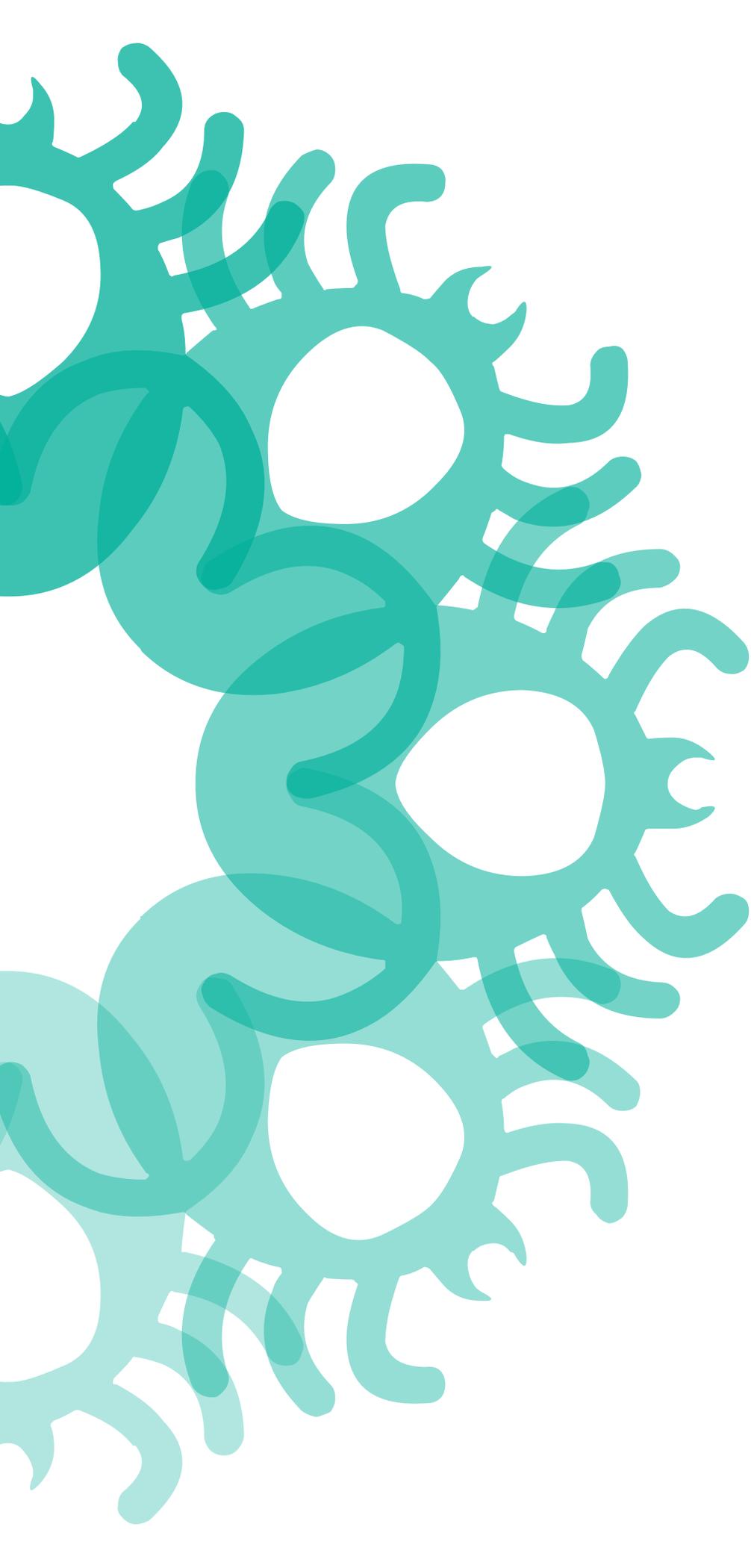
Lapisa®



Exterminate **them from inside.**

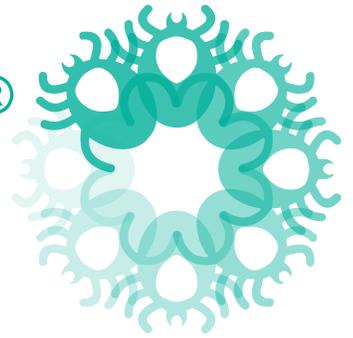
***Bovimune***  
**ixovac**® 

The **vaccine** against **ticks**



Exterminate **them from inside.**

# *Bovimune* **ixovac**<sup>®</sup>

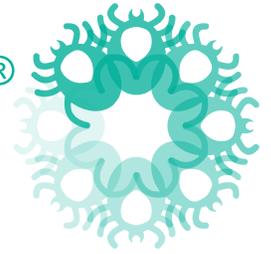


The **vaccine** against **ticks**



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# **Bovimune** **ixovac**<sup>®</sup>



Recombinant vaccine coadjuvant for the control  
of the tick *Rhipicephalus (Boophilus) microplus* spp.

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## 1. 1. The resistance of the cattle tick *Rhipicephalus (Boophilus) microplus* in Mexico



The resistance of the ticks to commonly used acaricides in one or three hosts is a serious problem that threatens livestock in tropical and subtropical regions around the world. In most of the Latin American countries, this phenomenon has been reported and mainly in ticks *Rhipicephalus (Boophilus) microplus*. Even though 20 years ago, the control of ticks in Mexico had an important advance because of the use of long-lasting pyrethroids; in the last 10 years, the situation has worsened considerably, due to the selection of the multi-resistant ticks population; because there are livestock areas where strains have been detected that are resistant to organophosphorus acaricides (Aguirre et al., 1986) to pyrethroids (Ortiz et al., 1995) to amitraz (Fragoso & Soberanes 2001; Soberanes et al., 2002) to ivermectin (Pérez et al., 2010) and to fipronil (Miller et al., 2013).

Most of the cattlemen in Mexico control tick by the periodical acaricide application of their livestock, and when they introduce a new product into their ranch, they are pleased to see the cleanliness of the animals. Nevertheless, is very common that as time passes they realize that they have to shorten the frequency of these acaricide treatments and they do not achieve this cleanliness, until finally they become desperate and change to another acaricide to seek greater effectiveness. This experience has been repeated for years over and over, so the idea of establishing control programs considering the susceptibility to insecticides and the behavior of ticks that particularly affects each region is increasingly urgent.

## 2. Immunological control

Due to the negative effects of acaricides over environment, public health and selection of resistant ticks, immunological control has become one of the most promising alternatives to fight these arthropods (Almazán et al., 2010), its advantages includes: it is easy to administer, friendly to environment, do not contaminate products destined to human consumption (meat and milk) they represent a better cost-benefit compared to the use of acaricides because of the reduction of treatments with commercial products and because the resistance to vaccination through selective adaptation, that is less probably to occurs compared to the acaricides (de la Fuente & Kocan, 2006; Nuttall et al., 2006; de la Fuente et al., 2007).

The different ways in which the immune system of the animals can act against ticks when Bm86 has been used as antigen, is based on three fundamental stages which are:

- Binding of the immunoglobulins to the digestive cells or target cells.
- Fixation of the complement that produces cell lysis and increasing the opsonization of the antibodies allowing the attack by phagocytes.
- Finally, inhibition of endocytosis as a consequence of the binding of antibodies (Tizard, 2009; Hope et al., 2010).

Bm86 protein isolated from the plasmatic membrane of epithelial cells of ticks intestine *R. (B.) microplus*, was cloned by recombinant DNA technology and expressed in *E. coli* in Australia (Kemp et al. 1986; Willadsen, 1989; Willadsen & Mckenna, 1991); later, in Cuba with the expression vector *Pichia pastoris* in which higher levels of purity of protein were obtained (Rodríguez et al., 1994; Canales et al., 2007; Canales et al., 2009) and recently in LAPISA, taking the germplasm of the Mexican strain of *R. (B.) microplus*, "Media

Joya" and cloned on the expression vector *Pichia pastoris*.

Prior to implementing the program, a diagnosis of resistance of cattle tick must be done in each ranch, in CENAPA or with the resistance field Kit that **Lapisa**'s representatives have.



### 3. Steps to implement the Integral Control Program with Bovimune Ixovac®

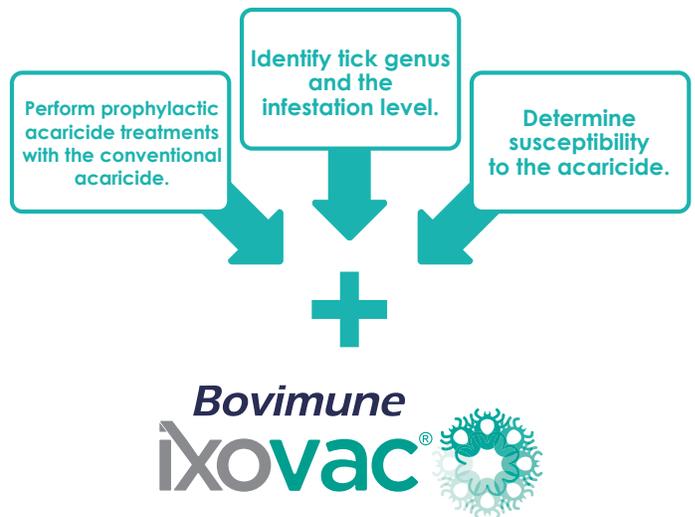
During the first three months after first vaccination, according to geographical area, season of the year and level of initial infestation of the cattle tick *R. (B.) microplus*, prophylactic acaricide treatments\* should be performed with the acaricide which is still effective in the ranch, whenever the cattle present an infestation of more than 30 \*\* semi-engorged ticks (4-8 mm) per side / animal. Same prophylactic acaricide treatments whose withdrawal will be gradual once the second and third vaccinations are applied and less infestation is observed in cattle, until 180 days (6 months) where revaccination with **Bovimune Ixovac®** will be done (table 1, figure 1) .

All cattle of the ranch must be vaccinated. If a new animal is incorporated, it has to be vaccinated and applied prophylactic acaricide treatments.

In young animals, the vaccination program must begin from the second month of age.

VACCINATION	WEEK
First Vaccination	Week 0
Second Vaccination	4th week
Third Vaccination	7th week
Revaccination	6th month from the beginning

**Table 1.** Vaccination program with 3 immunizations with **Bovimune Ixovac®** and revaccinations (every 6 months).



**Figure 1.** Integral Control Program with **Bovimune Ixovac®**.



\* Prophylactic acaricide treatments are done when the ticks' infestation levels exceed the productive economic threshold.

\*\* Ticks' economic threshold

# INTEGRAL CONTROL PROGRAM

## Gradual REDUCTION of larval infestation

Previous steps to implement the program

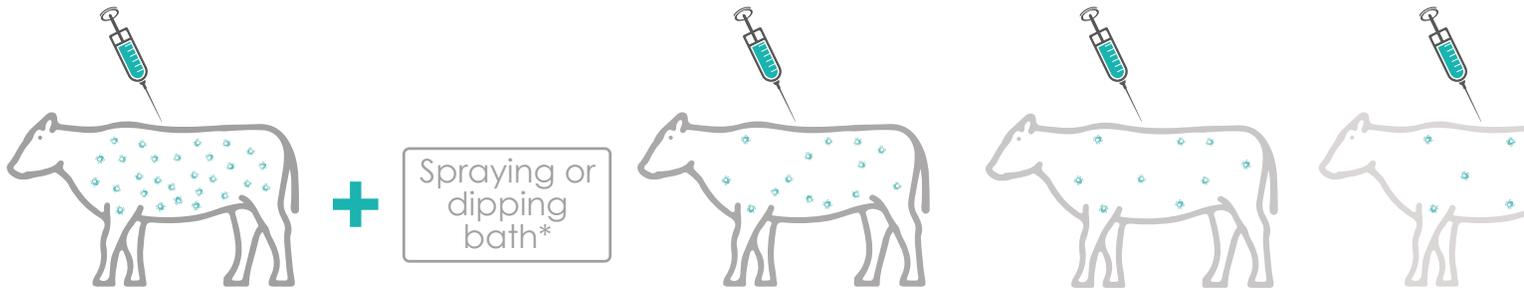


Which tick genus do I have in my cattle?

CENAPA or Lapis's field Kit

To which chemical family of acaricide is resistant?

Effect of **Bovimune IXOVA**



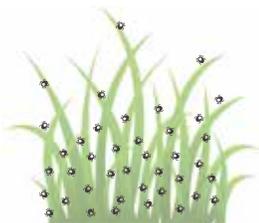
1st Vaccination (Week 0)

2nd Vaccination (4th week)

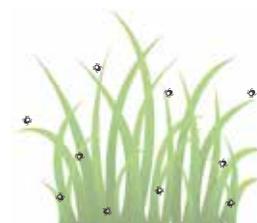
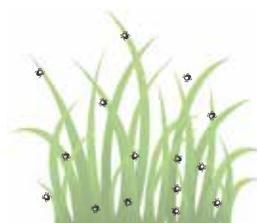
3rd Vaccination (7th week)

Revaccination (6th month from the beginning)

\*PROPHYLACTIC ACARICIDE TREATMENTS: Bovines with more than 30 ticks per side / animal



High larval infestation



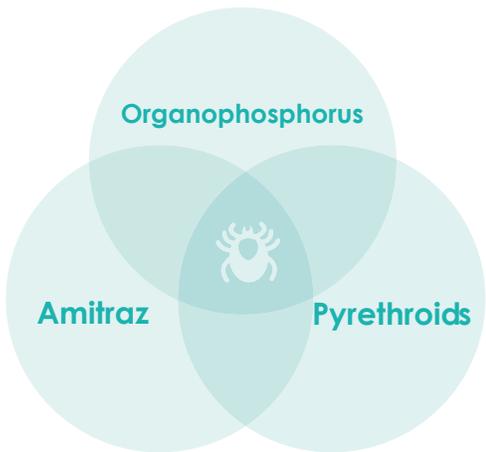
GRADUAL REDUCTION OF LARVAL INFESTATION

# GRAM WITH

## estations in animals and pastures

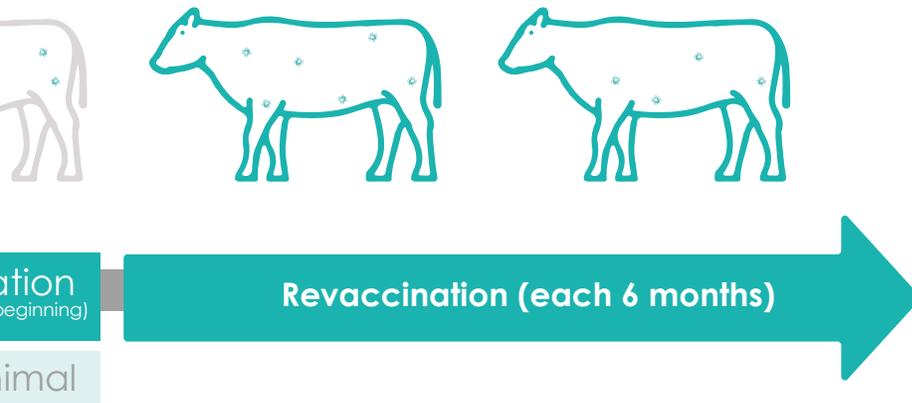
gram with **Bovimune IXOVAC**<sup>®</sup>

### ACARICIDES



Choose the most effective acaricide or the one with higher% of larval mortality

C<sup>®</sup> in animals and pastures

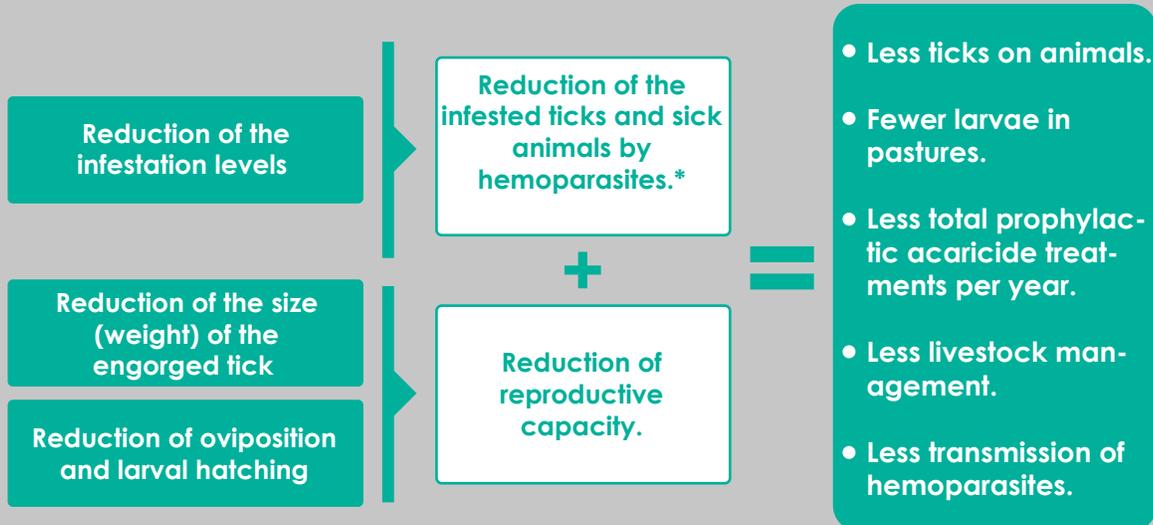
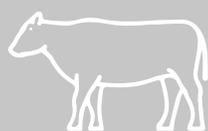


Less ticks in animals

Long-term sustainable control



Less ticks in pastures



\*Piroplasmosis y Anaplasmosis.

### 3.1. Why **Bovimune Ixovac**®?

### 3.2. How to begin the Integral Control Program?

The mechanism of action of **Bovimune Ixovac**®, has a cumulative effect in mid and long term, in the repletion of parasitic phases of tick *R. (B.) microplus* (larva, nymph, and young adults) and specially in the reproductive processes like fertility, egg survival and larvae of females that have been feeded from vaccinated animals. Its use within an Integral Control Program is needed to considerably reduce infestation levels of ticks on pastures and cattle.

The establishment of this program does not expect the complete elimination of ticks, instead a gradual increase of prophylactic acaricide treatments frequency, because the decrease of the infestation levels in pastures and bovines, without compromising health or productive and reproductive parameters of the animals, and guaranteeing the enzootic stability to hemoparasites (piroplasmosis and anaplasmosis).



## 4. Expectatives and some considerations

The implementation of the Integral Control Program of the cattle tick *R. (B.) microplus* with **Bovimune Ixovac®**, allows handling and gradually increasing the prophylactic acaricide treatments schedule with the acaricide of conventional application (spraying or dipping bath).

Combination of treatments will depend on the season of the year in which it starts, but a good beginning in tropical and subtropical zones of the country, is the application of **Bovimune Ixovac®** and a general acaricide treatments of cattle at the beginning of spring, the aim is the gradually decrease of population of larvae of ticks from the first generation of *R. (B.) microplus*.

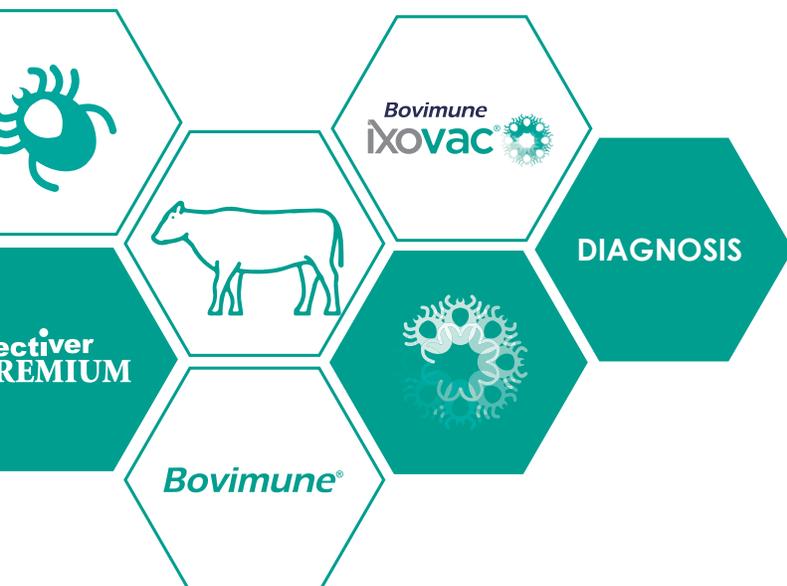
In case that the handle of cattle becomes complicated to apply prophylactic acaricide treatments, the use of **Dectiver® Premium** simultaneously with the first vaccination with **Bovimune Ixovac®** will be recommended, this with the aim of bringing down the first population of the year, which would favor keeping a tick level below the threshold of 30 ticks on cattle per side and reducing the following population peaks.

Use of an application of **Dectiver® Premium** during summer is convenient because its endectocide effect, furthermore, is the season with most abundance of infected larvae of gastrointestinal nematodes in pastures.

With the aim of reducing population of ticks to compatible levels with cattle production at an adequate cost, and considering premises previously defined, some basic recommendations to achieve success in the control of an operation:

- To establish a maximum tolerable level of 30 semi-engorged ticks (4 to 8 mm) per side / animal and 100 average horn flies per side / animal in the herd. Studies in Mexico and other countries have defined that these quantities per animal can be a reasonable productive economic threshold of tolerance.
- Lean on the professional representative or in the technical department of **LAPISA**, to identify the genus of ticks that are found on your cattle and determinate susceptibility of this to different chemical families of acaricides.
- At beginning of spring, which is normally a time of low infestation, apply the Integral Control Program with the vaccination scheme with **Bovimune Ixovac®** to all cattle. This program works as prophylactic and reduce challenges with larvae phases of ticks that tend to increase at this season. If it is applied in a correct and opportune way, it limits the quantity of ticks in following population generations. If loading conditions of ticks requires, because they reach in average more than 30 ticks semi-engorged per side / animal, apply treatment to 100% of animals, but if it is not, make prophylactic acaricide treatment to animals which exceed this tick's threshold.

These recommendations cannot be concluded, without mention the importance of other management and production measures that can help improving health condition and productivity of cattle, such as proper grazing practices, application of adequate programs of preventive medicine (vaccines and bacterines required according the zone), following biosecurity measures and control of the entrance of new animals, also nutritional supplementation with minerals that your DVM or nutritionist (Lapisa's Animal Nutrition) recommends.



## 5. Bovimune Ixovac® DOES NOT act as a knock-down acaricide

The effect of the vaccine is not the same as the one of a conventional application acaricide (spraying or dipping bath), also, it does not act like a conventional prophylactic vaccine. This vaccine induces an immune response in bovines which affects the repletion of ticks and its reproductive potential.

As a result, adult females that have been engorged in immunized animals fall to pastures and oviposit less eggs and in turn, larvae that hatch from them have less viability.

This effect is accumulative and therefore a progressive reduction is achieved from tick's population in pastures, which obtains big savings for less management, less acaricide treatments (contamination, resistance generation, etc.) and reduction of morbidity and mortality by hemoparasites transmitted by ticks.



## 6. Is Bovimune Ixovac® used also against hemoparasites?

**NO.** Control of hemoparasites illness (Anaplasmosis and Piroplasmosis) constitutes an aggregated value of **Bovimune Ixovac®** applied with Integral Control Program of cattle's tick. The established control against hemoparasites is associated to decrease of ticks also as other biosecurity measures that complement the

program. Although it has been reported that the antigen of tick interferes in transmission of hemoparasites and currently the mechanisms of interference are been studied.

## 7. Is **Bovimune Ixovac**<sup>®</sup> safe in lactating and pregnant cows?

It is a safe vaccine, can be applied in bovines from the second month of age, any breed, sex or productive state. It is safe for human, cattle, and environment, because it does not contaminate milk, meat or environment. Can be used with any acaricide whatever its active ingredient is (organophosphorus, pyrethroid, amidine, macrocyclic lactone), or its application method (spraying, dipping bath, pour on, injectable). It is even necessary that in addition to vaccination with **Bovimune Ixovac**<sup>®</sup>, prophylactic acaricide treatments continue, which will be less frequent.

## 8. Annex

### 8.1. Fast guide: Integral Control Program for cattle tick *R. (B.) microplus* with **Bovimune Ixovac**<sup>®</sup>



1. **Bovimune Ixovac**<sup>®</sup> does not eliminate by itself the totality of cattle's ticks; its use must be part of Integral Control Program.
2. Confirm the presence of bovine's tick *R. (B.) microplus* in cattle.
3. Perform resistance diagnosis test to acaricides at CENAPA or with field kit of the **LAPISA**'s representatives, to determinate the acaricide to use to which tick is susceptible or present less resistance.
4. Three vaccinations must be done at week 0, 4th and 7th.
5. Revaccinations must be applied each six months whatever if cattle has or not ticks.
6. At the beginning of the program is necessary vaccinating totality of animals starting with those older than 2 months. No animal should be left unvaccinated because it will affect the

rest of the herd.

7. When new animals are incorporated into the ranch, these must be vaccinated and applied acaricide treatments before grazing with the rest of the herd.
8. The application of **Bovimune Ixovac**<sup>®</sup>, can begin at any season of the year, nevertheless, is suggested that if is known the season in which less quantity of ticks in animals and in pastures are observed, it is recommended to apply vaccination program with **Bovimune Ixovac**<sup>®</sup> from 3 to 4 weeks previous to that period to obtain better results.
9. **Bovimune Ixovac**<sup>®</sup>, as any biological, produces its best effect in animals with good health and feeding.
10. Due to the first effects of **Bovimune Ixovac**<sup>®</sup> are observed from ticks' first generation exposed to vaccine, prophylactic acaricide treatments must continue during first three vaccinations. The extension of prophylactic acaricide treatments intervals will be decided from third vaccination, depending on animals' infestation levels. It is recommended to applied prophylactic acaricide treatments only those animals which have more than 30 semi-engorged ticks (4 to 8 mm) per side / animal.
11. If high infestations with *Amblyomma mixtum* (Almazan et al., 2016) are detected, will perform four prophylactic acaricide treatments weekly to reduce quickly the infestation with this specie.

8.2. Calendar for the Integral Control Program of the cattle tick with **Bovimune Ixovac®**

**Ranch:** \_\_\_\_\_ **Date:** \_\_\_\_\_

**State and town:** \_\_\_\_\_ **Dipping Bath:**

**Owner:** \_\_\_\_\_ **Spraying Bath:**

**Breed:** \_\_\_\_\_ **Location:** \_\_\_\_\_

**Tick's genus:** \_\_\_\_\_

MONTH	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEPT	OCT	NOV	DEC
DATE	<input type="checkbox"/>											
PROGRAM DAY	<input type="checkbox"/>											
EVENT	<input type="checkbox"/>											
< 10 ticks* <i>R. (B.) microplus</i>	<input type="checkbox"/>											
10 to 30 ticks* <i>R. (B.) microplus</i>	<input type="checkbox"/>											
30 a 40 ticks* <i>R. (B.) microplus</i>	<input type="checkbox"/>											
40 a 60 ticks* <i>R. (B.) microplus</i>	<input type="checkbox"/>											
> 60 ticks* <i>R. (B.) microplus</i>	<input type="checkbox"/>											

\*Semi-engorged ticks (4-8 mm) per side / animal.

Adviser

Technician

## 9. Consulted Literature

- Aguirre, E.J.; Santamaría, V.M. 1986. Purificación y caracterización toxicológica de garrapatas *Boophilus microplus* resistentes a ixodicidas organofosforados y organoclorados. Memorias de la VII Reunión Anual Asoc. Mex. de Parasitología Veterinaria, A.C. Cd. Victoria, Tamps.
- Almazan, C., Lagunes, R., Villar, M., Canales, M., Rosario-Cruz, R., Jongejan, F., de la Fuente, J. 2010. Identification and characterization of *Rhipicephalus (Boophilus) microplus* candidate protective antigens for the control of cattle tick infestations. Parasitol. Res. 106, 471-479.
- Almazan, C., Torres, T.A., Torres, R.L., Soberanes, C.N. y Ortiz, E.M. 2016. Aspectos biológicos de *Amblyomma mixtum* (Koch, 1844) en el noreste de México. Quehacer Científico en Chiapas. 11 (2).
- Canales, M., Enríquez, A., Ramos, E., Cabrera, D., Dandie, H., Soto, A., et al., 2007. Large -scale production in *Pichia pastoris* of the recombinant vaccine Gavac™ against cattle ticks. Vaccine. 15: 414-22.
- Canales, M., Almazan, C., Naranjo, V., Jongejan, F., de la Fuente, J. 2009. Vaccination with recombinant *Boophilus annulatus* Bm86 ortholog protein, Ba86, protects cattle against *B. annulatus* and *B. microplus* infestations. BMC Biotechnol. 9,29.
- de la Fuente, J., Kocan, K.M. 2006. Strategies for development of vaccines for control of ixodid tick species. Parasite Immunology. 28: 275-283.
- de la Fuente, J., Almazan, C., Canales, M., Perez de la Lastra, J.M., Kocan, K.M., Willadsen, P. 2007. A ten - year review of commercial vaccine performance for control of tick infestations on cattle. Anim. Health Res. Rev. 8, 23-28.
- Fragoso, S.H., Soberanes, C.N. 2001. Control de la resistencia a los ixodicidas a la luz de los conocimientos actuales. En: Memorias del XXV Congreso Nacional de Buiatría. Asociación Mexicana de Médicos Especialistas en Bovinos, A.C. Ed. Del 16 al 18 de agosto de 2001. Veracruz, Veracruz, México. pp. 40-48.
- Hope M, Jiang X, Gough J, Cadogan L, Josh P, Jonsson N, Willadsen P. 2010. Experimental vaccination of sheep and cattle against tick infestation using recombinant 5'- nucleotidase. Parasite Immunol; 32: 135-142.
- Kemp, D.H., Agbede, R.I.S., Johnston, L.A.Y. & Gough, J.M. 1986. Immunization of cattle against *Boophilus microplus* using extracts derived from adult female ticks: Feeding and survival of the parasite on vaccinated cattle. Int. J. Parasitol. 16:115-120.
- Miller RJ, Almazan C., Ortiz-Estrada M, Davey RB, George JE, De León AP. 2013. First report of fipronil resistance in *Rhipicephalus (Boophilus) microplus* of Mexico Vet. Parasitol; 191: 97-101.
- Nuttall P. A., Trimmell A. R., Kazimirova M., Labuda M. 2006. Exposed and concealed antigens as vaccine targets for controlling ticks and tick-borne diseases. Parasite Immunol. 28, 155-163.
- NOM-006-ZOO-1994. Requisitos de efectividad biológica para ixodicidas de uso en bovinos y método de prueba.
- Ortiz E.M, Santamaría V.M, Ortiz N.A, Soberanes C.N, Osorio M.J, Franco B.R, Martínez I.F, Quezada D.R, Fragoso S.H. 1995. Caracterización de la resistencia de *B. microplus* a ixodicidas en México. Memorias del III Seminario Internacional de Parasitología Animal. SAGAR-CANIFARMA-FAO-ICA-INIFAP. Acapulco, Gro. Méx. 1995: 58-66.
- Pérez- Cogollo LC., Rodríguez- Vivas RJ., Ramírez- Cruz GT., Miller RJ. 2010. First report of the cattle tick *Rhipicephalus microplus* resistant to ivermectin in Mexico Vet. Parasitol. 168: 165-169.
- Reporte técnico de la Evaluación biológica de la vacuna experimental PBvac-M50 contra la garrapata *Rhipicephalus (B.) microplus* en bovinos naturalmente infestados. 2016. No. de estudio: Garrapata PC03/14. CENAPA-SENASICA.
- Rodríguez M, Rubiera R, Penichet M, Montesinos R, Cremata J, et al. 1994. High level expression of the *B. microplus* Bm86 antigen in the yeast *P. pastoris* forming highly immunogenic particles for cattle. J. of Biotech. 33: 135 - 146.
- Soberanes C.N., Santamaría V.M., Fragoso S.H. y García V.Z. 2002. Primer caso de resistencia al Amitraz en la garrapata del ganado *B. microplus* en México. Tec. Pec. Mex. 40 (1): 81-92.
- Tizard, I.R. 2009. Veterinary Immunology. An Introduction. 8th edition. Elsevier.
- Willadsen, P, Riding GA, McKenna RV, Kemp DH, Tellam RL, Nielsen JN, Lahstein J, Cobon GS, Gough JM. 1989. Immunological control of a parasitic arthropod: identification of a protective antigen from *Boophilus microplus*. J Immunol. 143:1346-1351.
- Willadsen, P, McKenna, R.V. 1991. Vaccination with 'concealed' antigens: myth or reality?. Parasite Immunol. 13 (6): 605-16.



## DESCRIPTION:

Recombinant vaccine coadjuvant indicated for the control in infestations by ticks *Rhipicephalus* (*Boophilus*) spp.

## FORMULA:

Each dose of 2 mL contains:  
120 ± 20 µg of antigen rBm86 of *Rhipicephalus* (*Boophilus*) spp. in oily adjuvant.

## INDICATIONS AND USAGE:

Recombinant vaccine coadjuvant indicated for the control in infestations by ticks *Rhipicephalus* (*Boophilus*) spp.; for use in bovines from 2 months of age at any productive stage, keeping vaccination program without interruptions, combining with acaricide treatments.

## DOSAGE:

In bovines from 2 months of age: 2 mL per animal. Treatment includes a dose in weeks 0, 4, 7 and reinforcement of one dose every 6 months.

## ADMINISTRATION:

Intramuscular.

Bovimune Ixovac® is a recombinant vaccine coadjuvant indicated for the control of tick *Rhipicephalus* (*Boophilus*) spp. resistant to ixodicides organophosphorus, pyrethroids, amitraz and/or fipronil by the active immunization of bovines.

Bovimune Ixovac® must be used with an Integral Control Program in combination with acaricides of conventional use.

## WARNINGS:

Withdrawal time in meat and milk: 0 days.

Store refrigerated at 2 – 8°C.

Do not freeze. Protect from light.

Shake the product well before using.

Once the bottle is opened, the product must be used complete.

Do not reuse the bottle, destroy it.

Destroy the empty container by burring or incinerating and dispose of it in a safe manner.

Keep out for the reach of children and domestic animals.

Only for veterinary use.

## PRESENTATIONS:

20 mL (10 doses), 100 mL (50 doses).

## CONSULT A VETERINARY VETERINARY USE

Exterminate **them from inside.**

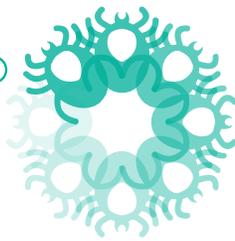
**Bovimune**  
**ixovac**® 

The **vaccine** against **ticks**



REGISTRO SAGARPA B-2083-031

***Bovimune***  
**ixovac**<sup>®</sup>



**Made in Mexico for:**

**LAPISA, S.A. DE C.V.**

Carr. La Piedad-Guadalajara. Km. 5.5,

Col. Camelinas, C. P. 59375,

La Piedad, Michoacán, México.

Tel +52 (352) 526-13-00

[www.lapisa.com](http://www.lapisa.com)

